The printed trachea

Vivekkumar Patel, Bryan M. Burt

Division of Thoracic Surgery, The Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX, USA *Correspondence to:* Bryan M. Burt, MD, FACS. Division of Thoracic Surgery, The Michael E. DeBakey Department of Surgery, Baylor College of Medicine, One Baylor Plaza, MS: BCM 390, Houston, TX 77030, USA. Email: bryan.burt@bcm.edu.

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Comment on: Rehmani SS, Al-Ayoubi AM, Ayub A, *et al.* Three-Dimensional-Printed Bioengineered Tracheal Grafts: Preclinical Results and Potential for Human Use. Ann Thorac Surg 2017;104:998-1004.

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In an effort to provide a novel option for tracheal reconstruction, Rehmani *et al.* demonstrate the successful use of a composite 3D bioengineered tracheal graft in porcine models for clinical use in patients with long segment tracheal defects (1). Historically, grafts such as silicone tubes, dermal grafts, polytetrafluoroethylene (PTFE) grafts, aortic allograft, and cadaveric grafts have enjoyed limited success due to lack of availability, size mismatch, poor vascularization, stenosis, and potential need for immunosuppression (2,3). Nevertheless, recent advances in bioengineering have made it possible to create a customized conduit that has the dynamic rigidity and flexibility of the trachea.

In their translational study utilizing a porcine model (n=7), Rehmani et al. illustrate use of a composite graft constructed of 3D printed polycaprolactone (PCL) C-rings, which provide tensile strength; and a bovine dermal collagen extracellular matrix, which provides a flexible stratum for epithelialization, mucosal coverage, and cellular recruitment. First, the authors show that PCL, a popular biodegradable synthetic material that may be customized to size and shape by 3D fusion deposition printing, is a compatible substrate for human mesenchymal stem cell (hMSC) growth in vitro, and therefore would allow for cell growth and good engraftment with host tissue (4,5). Next, the authors demonstrate that preoperative CT scanning may be used to generate customized 3D printed PCL C-rings to attach to the dermal collagen matrix for implantation as a composite tracheal graft. Following creation of an anterior tracheal defect (4 cm × 1.6 cm), seven animals underwent patch repair with the composite graft. Bronchoscopy performed at 1 and 3 months postoperatively in the 5 out of 7 surviving animals confirmed patent tracheal lumens, luminal mucosal coverage, and vascularization as evidenced by surface capillaries. Good engraftment with no dehiscence was noted at autopsy in all surviving animals. Furthermore, histology demonstrated epithelialization of the lumen as well as the presence of cilia and goblet cells. One animal died from airway stenosis due to intraluminal granulation tissue and another from pneumonia.

Compared to previously available options, Rehmani's composite PCL-ECM graft seems very appealing given its customizability, pliable yet rigid structural design similar to the trachea and good integration with native trachea. While this study represents a great initial pilot study to examine the feasibility and application of a new bioengineered product, a much more intensive investigation of tracheal grafts is still necessary prior to clinical use. First, longer term follow-up of animal models in a larger cohort would certainly be necessary to assess long term engraftment and integration with native tissue. Next, immunogenicity of these bioengineered grafts and the potential for rejection has not been formally evaluated. Immunohistochemistry of implanted grafts may be helpful in assessing the degree of inflammatory response generated by the biosynthetic materials. Furthermore, given the numerous new bioengineered tracheal grafts available, including one seeded with mesenchymal stem cells proposed by Rehmani's group, a direct comparison of these grafts would be valuable to elicit differences in structural integrity, immunogenicity,

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long term engraftment and vascularization (5-7).

Whereas the gold standard for tracheal reconstruction remains tracheal mobilization and reconstruction instead of replacement (8,9), many thoracic surgeons have been presented with difficult cases for which reconstruction is not possible, and for which a durable option for replacement is required. Thus, Rehmani *et al.*'s iteration of a replacement tracheal graft signifies a formative step forward given in the search for a feasible tracheal replacement that has been ongoing since the early 1900's.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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